

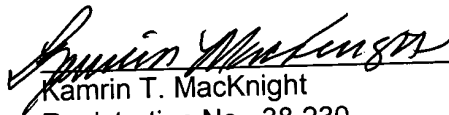
### REMARKS

In the present Preliminary Amendment, originally filed Claims 1-14 have been canceled and new Claims 15-29 have been added. Applicants respectfully request that these newly added Claims be examined in the present Continuation application. Applicants reserve the right to pursue Claims based on canceled Claims 1-14 in any subsequently filed Divisional and/or Continuation application(s). It is not intended that these amendments narrow the scope of any of the amended Claims within the meaning of *Festo*<sup>1</sup>. (protease are tested). The amendments to the Drawings have been made in order to more clearly present Figures 7 and 8 and meet the drawing requirements of CFR §1.84. Applicant submits that these amendments find more than sufficient support in the Specification. No new matter has been added in these amendments.

Should the Examiner have any questions or if a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

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<sup>1</sup> *Festo Corp. v. Shoketsu Kogyo Kabushiki Co.*, No. 95-1066, 2000 WL 1753646 (Fed. Cir. Nov. 29, 2000).

**APPENDIX I**

Replacement drawing sheets for Figures 7 and 8 are attached hereto.

Residues 135 – 149 of SEQ ID NO:3	2	A11	LEQAVNSATSRGVLV
Residues 1 – 15 of SEQ ID NO:3	3	A10	AQSVPWGISRVQAPA
Residues 4 – 18 of SEQ ID NO:3	4	A9	VPWGISRVQAPAAHN
Residues 7 – 21 of SEQ ID NO:3	5	A8	GISRVQAPAAHNRGL
Residues 10 – 24 of SEQ ID NO:3	6	A7	RVQAPAAHNRGLTGS
Residues 13 – 27 of SEQ ID NO:3	7	A6	APAAHNRGLTGSGVK
Residues 16 – 30 of SEQ ID NO:3	8	A5	AHNRGLTGSGVKVAV
Residues 19 – 33 of SEQ ID NO:3	9	A4	RGLTGSGVKVAVLDT
Residues 22 – 36 of SEQ ID NO:3	10	A3	TGSGVKVAVLDTGIS
Residues 25 – 39 of SEQ ID NO:3	11	A2	GVKVAVLDTGISTHP
Residues 28 – 42 of SEQ ID NO:3	12	A1	VAVLDTGISTHPDLN
Residues 31 – 45 of SEQ ID NO:3	13	B12	LDTGISTHPDLNIRG
Residues 34 – 48 of SEQ ID NO:3	14	B11	GISTHPDLNIRGGAS
Residues 37 – 51 of SEQ ID NO:3	15	B10	THPDLNIRGGASFVP
Residues 40 – 54 of SEQ ID NO:3	16	B9	DLNIRGGASFVPGEP
Residues 43 – 57 of SEQ ID NO:3	17	B8	IRGGASFVPGEPSTQ
Residues 46 – 60 of SEQ ID NO:3	18	B7	GASFVPGEPSTQDGN
Residues 49 – 63 of SEQ ID NO:3	19	B6	FVPGEPSTQDGNHGH
Residues 52 – 66 of SEQ ID NO:3	20	B5	GEPSTQDGNHGHGTHV
Residues 55 – 69 of SEQ ID NO:3	21	B4	STQDGNHGHGTHVAGT
Residues 58 – 72 of SEQ ID NO:3	22	B3	DGNHGHGTHVAGTIAA
Residues 61 – 75 of SEQ ID NO:3	23	B2	GHGTHVAGTIAALNN
Residues 64 – 78 of SEQ ID NO:3	24	B1	THVAGTIAALNNSIG
Residues 67 – 81 of SEQ ID NO:3	25	C12	AGTIAALNNSIGVLG
Residues 70 – 84 of SEQ ID NO:3	26	C11	IAALNNSIGVLGVAP
Residues 73 – 87 of SEQ ID NO:3	27	C10	LNNSIGVLGVAPSAE
Residues 76 – 90 of SEQ ID NO:3	28	C9	SIGVLGVAPSAELYA
Residues 79 – 93 of SEQ ID NO:3	29	C8	VLGVAPSAELYAVKV
Residues 82 – 96 of SEQ ID NO:3	30	C7	VAPSAELYAVKVLGA
Residues 85 – 99 of SEQ ID NO:3	31	C6	SAELYAVKVLGASGS
Residues 88 – 102 of SEQ ID NO:3	32	C5	LYAVKVLGASGSGSV
Residues 91 – 105 of SEQ ID NO:3	33	C4	VKVLGASGSGSVSSI
Residues 94 – 108 of SEQ ID NO:3	34	C3	LGASGSGSVSSIAQG
Residues 97 – 111 of SEQ ID NO:3	35	C2	SGSGSVSSIAQGLEW
Residues 100 – 114 of SEQ ID NO:3	36	C1	GSVSSIAQGLEWAGN
Residues 103 – 117 of SEQ ID NO:3	37	D12	SSIAQGLEWAGNNGM
Residues 106 – 120 of SEQ ID NO:3	38	D11	AQGLEWAGNNGMHVA
Residues 109 – 123 of SEQ ID NO:3	39	D10	LEWAGNNGMHVANLS
Residues 112 – 126 of SEQ ID NO:3	40	D9	AGNNGMHVANLSLGS
Residues 115 – 129 of SEQ ID NO:3	41	D8	NGMHVANLSLGSPSP

FIG. 7A

Residues 118 – 132 of SEQ ID NO:3	42	D7	HVANLSLGSPSPSAT
Residues 121 – 135 of SEQ ID NO:3	43	D6	NLSLGSPSPSATLEQ
Residues 124 – 138 of SEQ ID NO:3	44	D5	LGSPSPSATLEQAVN
Residues 127 – 141 of SEQ ID NO:3	45	D4	PSPSATLEQAVNSAT
Residues 130 – 144 of SEQ ID NO:3	46	D3	SATLEQAVNSATSRG
Residues 133 – 147 of SEQ ID NO:3	47	D2	LEQAVNSATSRGVLV
Residues 136 – 150 of SEQ ID NO:3	48	D1	AVNSATSRGVLVVAA
Residues 139 – 153 of SEQ ID NO:3	49	E12	SATSRGVLVVAASGN
Residues 142 – 156 of SEQ ID NO:3	50	E11	SRGVLVVAASGNSGA
Residues 145 – 159 of SEQ ID NO:3	51	E10	VLVVAASGNSGAGSI
Residues 148 – 162 of SEQ ID NO:3	52	E9	VAASGNSGAGSISYP
Residues 151 – 165 of SEQ ID NO:3	53	E8	SGNSGAGSISYPARY
Residues 154 – 168 of SEQ ID NO:3	54	E7	SGAGSISYPARYANA
Residues 157 – 171 of SEQ ID NO:3	55	E6	GSISYPARYANAMAV
Residues 160 – 174 of SEQ ID NO:3	56	E5	SYPARYANAMAVGAT
Residues 163 – 177 of SEQ ID NO:3	57	E4	ARYANAMAVGATDQN
Residues 166 – 180 of SEQ ID NO:3	58	E3	ANAMAVGATDQNNNR
Residues 169 – 183 of SEQ ID NO:3	59	E2	MAVGATDQNNNRASF
Residues 172 – 186 of SEQ ID NO:3	60	E1	GATDQNNNRASFQY
Residues 175 – 189 of SEQ ID NO:3	61	F12	DQNNNRASFQYGAG
Residues 178 – 192 of SEQ ID NO:3	62	F11	NNRASFSQYGAGLDI
Residues 181 – 195 of SEQ ID NO:3	63	F10	ASFSQYGAGLDIVAP
Residues 184 – 198 of SEQ ID NO:3	64	F9	SQYGAGLDIVAPGVN
Residues 187 – 201 of SEQ ID NO:3	65	F8	GAGLDIVAPGVNVQS
Residues 190 – 204 of SEQ ID NO:3	66	F7	LDIVAPGVNVQSTYP
Residues 193 – 207 of SEQ ID NO:3	67	F6	VAPGVNVQSTYPGST
Residues 196 – 210 of SEQ ID NO:3	68	F5	GVNVQSTYPGSTYAS
Residues 199 – 213 of SEQ ID NO:3	69	F4	VQSTYPGSTYASLNG
Residues 202 – 216 of SEQ ID NO:3	70	F3	TYPGSTYASLNGTSM
Residues 205 – 219 of SEQ ID NO:3	71	F2	GSTYASLNGTSMATP
Residues 208 – 222 of SEQ ID NO:3	72	F1	YASLNGTSMATPHVA
Residues 211 – 225 of SEQ ID NO:3	73	G12	LNGTSMATPHVAGAA
Residues 214 – 228 of SEQ ID NO:3	74	G11	TSMATPHVAGAAALV
Residues 217 – 231 of SEQ ID NO:3	75	G10	ATPHVAGAAALVKQK
Residues 220 – 234 of SEQ ID NO:3	76	G9	HVAGAAALVKQKNPS
Residues 223 – 237 of SEQ ID NO:3	77	G8	GAAALVKQKNPSWSN
Residues 226 – 240 of SEQ ID NO:3	78	G7	ALVKQKNPSWSNVQI
Residues 229 – 243 of SEQ ID NO:3	79	G6	KQKNPSWSNVQIRNH
Residues 232 – 246 of SEQ ID NO:3	80	G5	NPSWSNVQIRNHLKN
Residues 235 – 249 of SEQ ID NO:3	81	G4	WSNVQIRNHLKNTAT
Residues 238 – 252 of SEQ ID NO:3	82	G3	VQIRNHLKNTATSLG

FIG. 7B

Residues 241 – 255 of SEQ ID NO:3	83	G2	RNHLKNTATSLGSTN
Residues 244 – 258 of SEQ ID NO:3	84	G1	LKNTATSLGSTNLYG
Residues 247 – 261 of SEQ ID NO:3	85	H12	TATSLGSTNLYGSGL
Residues 250 – 264 of SEQ ID NO:3	86	H11	SLGSTNLYGSGLVNA
Residues 253 – 267 of SEQ ID NO:3	87	H10	STNLYGSGLVNAEAA
Residues 256 – 270 of SEQ ID NO:3	88	H9	NLYGSGLVNAEAATR

FIG. 7C

Residues 269 – 283 of SEQ ID NO:6	2	A11	DAELHIFRVFTNNQV
Residues 161 – 175 of SEQ ID NO:6	3	A10	PLRRASLSLGSGFWH
Residues 164 – 178 of SEQ ID NO:6	4	A9	RASLSLGSGFWHATG
Residues 167 – 181 of SEQ ID NO:6	5	A8	LSLGSGFWHATGRHS
Residues 170 – 184 of SEQ ID NO:6	6	A7	GSGFWHATGRHSSRR
Residues 173 – 187 of SEQ ID NO:6	7	A6	FWHATGRHSSRLLR
Residues 176 – 190 of SEQ ID NO:6	8	A5	ATGRHSSRLLRAIP
Residues 179 – 193 of SEQ ID NO:6	9	A4	RHSSRLLRAIPRQV
Residues 182 – 196 of SEQ ID NO:6	10	A3	SRLLRAIPRQVAQT
Residues 185 – 199 of SEQ ID NO:6	11	A2	LLRAIPRQVAQTLQA
Residues 188 – 202 of SEQ ID NO:6	12	A1	AIPRQVAQTLQADV
Residues 191 – 205 of SEQ ID NO:6	13	B12	RQVAQTLQADVLWQM
Residues 194 – 208 of SEQ ID NO:6	14	B11	AQTLQADVLWQMGYT
Residues 197 – 211 of SEQ ID NO:6	15	B10	LQADVLWQMGYTGAN
Residues 200 – 214 of SEQ ID NO:6	16	B9	DVLWQMGYTGANVRV
Residues 203 – 217 of SEQ ID NO:6	17	B8	WQMGYTGANVRVAVF
Residues 206 – 220 of SEQ ID NO:6	18	B7	GYTGANVRVAVFDTG
Residues 209 – 223 of SEQ ID NO:6	19	B6	GANVRVAVFDTGLSE
Residues 212 – 226 of SEQ ID NO:6	20	B5	VRVAVFDTGLSEKHP
Residues 215 – 229 of SEQ ID NO:6	21	B4	AVFDTGLSEKHPHFK
Residues 218 – 232 of SEQ ID NO:6	22	B3	DTGLSEKHPHFKNVK
Residues 221 – 235 of SEQ ID NO:6	23	B2	LSEKHPHFKNVKERT
Residues 224 – 238 of SEQ ID NO:6	24	B1	KHPHFKNVKERTNWT
Residues 227 – 241 of SEQ ID NO:6	25	C12	HFKNVKERTNWTNER
Residues 230 – 244 of SEQ ID NO:6	26	C11	NVKERTNWTNERTLD
Residues 233 – 247 of SEQ ID NO:6	27	C10	ERTNWTNERTLDDGL
Residues 236 – 250 of SEQ ID NO:6	28	C9	NWTNERTLDDGLGHG
Residues 239 – 253 of SEQ ID NO:6	29	C8	NERTLDDGLGHGTFV
Residues 242 – 256 of SEQ ID NO:6	30	C7	TLDDGLGHGTFVAGV
Residues 245 – 259 of SEQ ID NO:6	31	C6	DGLGHGTFVAGVIAS
Residues 248 – 262 of SEQ ID NO:6	32	C5	GHGTFVAGVIASMRE
Residues 251 – 265 of SEQ ID NO:6	33	C4	TFVAGVIASMRECQG
Residues 254 – 268 of SEQ ID NO:6	34	C3	AGVIASMRECQGFAP
Residues 257 – 271 of SEQ ID NO:6	35	C2	IASMRECQGFAPDAE
Residues 260 – 274 of SEQ ID NO:6	36	C1	MRECQGFAPDAELHI
Residues 263 – 277 of SEQ ID NO:6	37	D12	CQGFAPDAELHIFRV
Residues 266 – 280 of SEQ ID NO:6	38	D11	FAPDAELHIFRVFTN
Residues 269 – 283 of SEQ ID NO:6	39	D10	DAELHIFRVFTNNOV

FIG. 8A

Residues 272 – 286 of SEQ ID NO:6	40	D9	LHIFRVFTNNQVSYT
Residues 275 – 289 of SEQ ID NO:6	41	D8	FRVFTNNQVSYTSWF
Residues 278 – 292 of SEQ ID NO:6	42	D7	FTNNQVSYTSWFLDA
Residues 281 – 295 of SEQ ID NO:6	43	D6	NQVSYTSWFLDAFNY
Residues 284 – 298 of SEQ ID NO:6	44	D5	SYTSWFLDAFNYAIL
Residues 287 – 301 of SEQ ID NO:6	45	D4	SWFLDAFNYAILKKI
Residues 290 – 304 of SEQ ID NO:6	46	D3	LDAFNYAILKKIDVL
Residues 293 – 307 of SEQ ID NO:6	47	D2	FNYAILKKIDVLNLS
Residues 296 – 310 of SEQ ID NO:6	48	D1	AILKKIDVLNLSIGG
Residues 299 – 313 of SEQ ID NO:6	49	E12	KKIDVLNLSIGGPDF
Residues 302 – 316 of SEQ ID NO:6	50	E11	DVLNLSIGGPDFMDH
Residues 305 – 319 of SEQ ID NO:6	51	E10	NLSIGGPDFMDHPFV
Residues 308 – 322 of SEQ ID NO:6	52	E9	IGGPDFMDHPFVDKV
Residues 311 – 325 of SEQ ID NO:6	53	E8	PDFMDHPFVDKVVWEL
Residues 314 – 328 of SEQ ID NO:6	54	E7	MDHPFVDKVVWELTAN
Residues 317 – 331 of SEQ ID NO:6	55	E6	PFVDKVVWELTANNVI
Residues 320 – 334 of SEQ ID NO:6	56	E5	DKVVWELTANNVIMVS
Residues 323 – 337 of SEQ ID NO:6	57	E4	WELTANNVIMVSAIG
Residues 326 – 340 of SEQ ID NO:6	58	E3	TANNVIMVSAIGNDG
Residues 329 – 343 of SEQ ID NO:6	59	E2	NVIMVSAIGNDGPLY
Residues 332 – 346 of SEQ ID NO:6	60	E1	MVSAIGNDGPLYGTJ
Residues 335 – 349 of SEQ ID NO:6	61	F12	AIGNDGPLYGTLNNP
Residues 338 – 352 of SEQ ID NO:6	62	F11	NDGPLYGTLNNPADQ
Residues 341 – 355 of SEQ ID NO:6	63	F10	PLYGTLNNPADQMDV
Residues 344 – 358 of SEQ ID NO:6	64	F9	GTLNNPADQMDVIGV
Residues 347 – 361 of SEQ ID NO:6	65	F8	NNPADQMDVIGVGGI
Residues 350 – 364 of SEQ ID NO:6	66	F7	ADQMDVIGVGGIDFE
Residues 353 – 367 of SEQ ID NO:6	67	F6	MDVIGVGGIDFEDNI
Residues 356 – 370 of SEQ ID NO:6	68	F5	IGVGGIDFEDNIARF
Residues 359 – 373 of SEQ ID NO:6	69	F4	GGIDFEDNIARFSSR
Residues 362 – 376 of SEQ ID NO:6	70	F3	DFEDNIARFSSRGMT
Residues 365 – 379 of SEQ ID NO:6	71	F2	DNIARFSSRGM TTWE
Residues 368 – 382 of SEQ ID NO:6	72	F1	ARFSSRGM TTWELPG
Residues 371 – 385 of SEQ ID NO:6	73	G12	SSRGM TTWELPGGYG
Residues 374 – 388 of SEQ ID NO:6	74	G11	GMTTWELPGGYGRMK
Residues 377 – 391 of SEQ ID NO:6	75	G10	TWELPGGYGRMKPDI
Residues 380 – 394 of SEQ ID NO:6	76	G9	LPGGYGRMKPDIVTY
Residues 383 – 397 of SEQ ID NO:6	77	G8	GYGRMKPDIVTYGAG
Residues 386 – 400 of SEQ ID NO:6	78	G7	RMKPDIVTYGAGVRG
Residues 389 – 403 of SEQ ID NO:6	79	G6	PDIVTYGAGVRGSGV

FIG. 8B

Residues 392 – 406 of SEQ ID NO:6	80	G5	VTYGAGVRGSGVKGG
Residues 395 – 409 of SEQ ID NO:6	81	G4	GAGVRGSGVKGGCRA
Residues 398 – 412 of SEQ ID NO:6	82	G3	VRGSGVKGGCRALSG
Residues 401 – 415 of SEQ ID NO:6	83	G2	SGVKGGCRALSGTSTV
Residues 404 – 418 of SEQ ID NO:6	84	G1	KGGCRALSGTSTVASP
Residues 407 – 421 of SEQ ID NO:6	85	H12	CRALSGTSTVASPVVA
Residues 410 – 424 of SEQ ID NO:6	86	H11	LSGTSTVASPVVAGAV
Residues 413 – 427 of SEQ ID NO:6	87	H10	TSVASPVVAGAVTLL
Residues 416 – 430 of SEQ ID NO:6	88	H9	ASPVVAGAVTLLVST
Residues 419 – 433 of SEQ ID NO:6	89	H8	VVAGAVTLLVSTVQK
Residues 422 – 436 of SEQ ID NO:6	90	H7	GAVTLLVSTVQKREL
Residues 425 – 439 of SEQ ID NO:6	91	H6	YLLVSTVQKRELVNP
Residues 428 – 442 of SEQ ID NO:6	92	H5	VSTVQKRELVNPASM
Residues 431 – 445 of SEQ ID NO:6	93	H4	VQKRELVNPASMKQA
Residues 434 – 448 of SEQ ID NO:6	94	H3	RELVNPASMKQALIA
Residues 437 – 451 of SEQ ID NO:6	95	H2	VNPASMKQALIASAR
Residues 440 – 455 of SEQ ID NO:6	96	H1	ASMKQALIASARRLP
Residues 269 – 283 of SEQ ID NO:6	98	I11	DAELHIFRVFTNNQV
Residues 443 – 457 of SEQ ID NO:6	99	I10	KQALIASARRLPGVN
Residues 446 – 460 of SEQ ID NO:6	100	I9	LIASARRLPGVNMF
Residues 449 – 463 of SEQ ID NO:6	101	I8	SARRLPGNMFEQGH
Residues 452 – 466 of SEQ ID NO:6	102	I7	RLPGVNMFEQGHGKL
Residues 455 – 469 of SEQ ID NO:6	103	I6	GVNMFEQGHGKLDLL
Residues 458 – 472 of SEQ ID NO:6	104	I5	MFEQGHGKLDLLRAY
Residues 461 – 475 of SEQ ID NO:6	105	I4	QGHGKLDLLRAYQIL
Residues 464 – 478 of SEQ ID NO:6	106	I3	GKLDLLRAYQILNSY
Residues 467 – 481 of SEQ ID NO:6	107	I2	DLLRAYQILNSYKPQ
Residues 470 – 484 of SEQ ID NO:6	108	I1	RAYQILNSYKPQASL
Residues 473 – 487 of SEQ ID NO:6	109	J12	QILNSYKPQASLAPS
Residues 476 – 490 of SEQ ID NO:6	110	J11	NSYKPQASLSPSYID
Residues 479 – 493 of SEQ ID NO:6	111	J10	KPQASLSPSYIDLTE
Residues 482 – 496 of SEQ ID NO:6	112	J9	ASLSPSYIDLTECPY
Residues 485 – 499 of SEQ ID NO:6	113	J8	SPSYIDLTECPYMW
Residues 488 – 502 of SEQ ID NO:6	114	J7	YIDLTECPYMWPYCS
Residues 491 – 505 of SEQ ID NO:6	115	J6	LTECPYMWPYCSQPI
Residues 494 – 508 of SEQ ID NO:6	116	J5	CPYMWPYCSQPIYYG

FIG. 8C



**APPENDIX II**  
**CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS AS**  
**AMENDED IN THIS COMMUNICATION**

The following is a list of the Claims as they would appear following entry of this amendment.

15. (New) A method for producing a mutant protease having reduced allergenicity comprising the steps of:
- a) obtaining a naturally-occurring protease having subtilisin activity and preparing fragments of said naturally-occurring protease having subtilisin activity;
  - b) contacting said fragments of said naturally-occurring protease with a first solution comprising naïve human CD4+ or CD8+ T-cells and dendritic cells, wherein said dendritic cells have been differentiated;
  - c) identifying an epitope region of said naturally-occurring protease, wherein said identifying comprises measuring the ability of said fragments of said naturally-occurring protease epitope region to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells;
  - d) replacing said epitope region identified in step c) with an analogous epitope region, to produce said mutant protease;
  - e) preparing fragments of said mutant protease;
  - f) contacting said fragments of said mutant protease with a second solution comprising naïve human CD4+ or CD8+ T-cells and dendritic cells, wherein said dendritic cells have been differentiated; and
  - g) measuring the ability of said fragments of said mutant protease to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells.
16. (New) The method of Claim 15, further comprising the step of comparing the ability of said fragments of said naturally-occurring protease having microbial subtilisin activity to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells with the ability of said fragments of said mutant protease to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells.

17. (New) The method of Claim 15, wherein said dendritic cells and said CD4+ or CD8+ T-cells in said first and second solutions are obtained from a single blood source.

18. (New) The method of Claim 15, wherein said naturally-occurring protease is obtained from a *Bacillus* selected from the group consisting of *B. amyloliquefaciens*, *B. subtilis*, *B. licheniformis*, *B. lentus*, and *Bacillus* PB92.

19. (New) The method of Claim 15, wherein said epitope is a T-cell epitope.

20. (New) The method of Claim 15, further comprising the step of producing an expression vector comprising a nucleic acid sequence encoding said mutant protease.

21. (New) The method of Claim 20, further comprising the step of transforming at least one host cell with said expression vector.

22. (New) The method of Claim 21, further comprising the steps of cultivating said at least one host cell in a culture medium under conditions that promote the expression of said mutant protease and recovering said mutant protease from said cell or said culture medium.

23. (New) A method for reducing the allergenicity of a microbial subtilisin comprising the steps of:

a) obtaining a microbial subtilisin, and preparing fragments of said microbial subtilisin;

b) contacting said fragments of said microbial subtilisin with a first solution comprising naïve human CD4+ or CD8+ T-cells and dendritic cells, wherein said dendritic cells have been differentiated;

c) identifying an epitope of said microbial subtilisin, wherein said identifying comprises measuring the ability of said fragments of said microbial subtilisin to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells;

- d) replacing said epitope identified in step c) with an analogous region to produce a mutant subtilisin;
- e) preparing fragments of said mutant subtilisin;
- f) contacting said fragments of said mutant subtilisin with a second solution comprising naïve human CD4+ or CD8+ T-cells and dendritic cells, wherein said dendritic cells have been differentiated; and
- g) measuring the ability of said fragments of said mutant subtilisin to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells, wherein at least one of said fragments of said mutant subtilisin stimulate said T-cells in said second solution to a lesser extent than the subtilisin in step c).

24. (New) The method of Claim 23, wherein said dendritic cells and said CD4+ or CD8+ T-cells in said first and second solutions are obtained from a single blood source.

25. (New) The method of Claim 23, wherein said subtilisin is obtained from a *Bacillus* selected from the group consisting of *B. amyloliquefaciens*, *B. subtilis*, *B. licheniformis*, *B. lentus*, and *Bacillus* PB92.

26. (New) The method of Claim 23, wherein said epitope is a T-cell epitope.

27. (New) The method of Claim 23, further comprising the step of producing an expression vector comprising a nucleic acid sequence encoding said mutant subtilisin.

28. (New) The method of Claim 27, further comprising the step of transforming at least one host cell with said expression vector.

29. (New) The method of Claim 28, further comprising the step of cultivating said at least one host cell in a culture medium under conditions that promote the expression of said mutant protease and recovering said mutant protease from said cell or said culture medium.